Drug Safety And Quality For Research Conducted Under An Radioactive Drug Research Committee (RDRC)

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Conditions for Research Under an RDRC

Radioactive Drugs for BASIC RESEARCH are generally recognized as safe and effective (GRASE) under the conditions set forth in 21 CFR 361.1

- **Committee consisting of qualified members, approved by the FDA, and responsible for reviewing and approving basic research studies.**
- **Limits on pharmacological dose.**
- **Limits on radiation dose.**
- **Use of drugs with prior human experience.**
- **Compliance with administrative and periodic reporting requirements.**

RDRC Defined Membership Requirements

21 CFR 361.1 (c) (1) *Membership*

A Radioactive Drug Research Committee shall consist of at least 5 individuals.

Each Committee shall include the following 3 individuals:

- **(i) a physician recognized as a specialist in nuclear medicine,**
- **(ii) a person qualified by training and experience to formulate radioactive drugs,**
- **(iii) a person with special competence in radiation safety and radiation dosimetry. …**

RDRC Responsibilities - Membership Reporting

21 CFR 361.1 (c) (4) *Approval* states

- **"Each Radioactive Drug Research Committee shall be specifically approved by the Center for Drug Evaluation and Research of the Food and Drug Administration. …**

- **… Changes in membership and applications for new members shall be submitted to the Food and Drug Administration as soon as, or before, vacancies occur on the committee."**

RDRC Responsibilities - Membership Functions

21 CFR 361.1 (c) (2) *Function* states

- **"… Each committee shall meet at least once each quarter in which research activity has been authorized or conducted. A quorum consisting of more than 50 percent of the membership must be present with appropriate representation of the required fields of specialization.**

- **Minutes shall be kept and shall include the numerical results of votes involving use in human subjects.**

- **No member shall vote on a protocol in which he is an investigator."**

Recent RDRC Experiences

Case 1

- **Administration of a labeled “biohazard”**
- **Inadequate process to clear viral contamination from human biologics (complete viral testing was not done)**
- **Informed consent did not state material was human-derived**

Case 2

- **Administration of an unknown compound**
- **Failure to follow established procedures during production of product**
- **Failure to perform quality controls prior to product administration**
- **Analytical equipment not maintained, nor calibrated for use**
- **Sterility tests are not conducted properly**

RDRC Responsibilities
Drug Quality and Purity
Questions an RDRC has to ask itself

How should our RDRC ensure protocols address:

- **Chemical integrity and purity of precursors for use in radiolabeling procedures?**
- **Changes made to established procedures suitable before being implemented in production of the product to be administered to humans?**
- **That the Radioactive drug molecule has correct identity?**

RDRC Responsibilities
Drug Quality and Purity
Questions an RDRC has to ask itself

How should our RDRC ensure protocols meet finished product testing:

- **Radiochemical and radionuclidic purity?**
- **Chemical purity?**
- **Specific activity (if pertinent)?**
- **Sterility and pyrogen-free?**
- **Adequacy of analytical procedures for finished product tests?**

Criteria for Determining Drug Safety and Quality

- **21 CFR 361.1 (c) (1) *Membership (ii)* requires each committee include "a person qualified by training and experience to formulate radioactive drugs,"**

- **21 CFR 361.1 (d) (7) *Research Protocol* requires the RDRC review a protocol which *IS* to address *ALL* requirements of section (d),**

Criteria for Determining Drug Safety and Quality

The RDRC must assure that the radioactive drug meets the following criteria [21 CFR 361.1(d)(6)]:

- **Appropriate chemical, pharmaceutical, radiochemical, and radionuclidic standards of strength, quality, and purity.**
- **Uniform and reproducible quality as to give significance to the research study conducted.**
- **Radioactive materials for parenteral use are prepared in sterile and pyrogen-free form.**

How to Achieve Drug Safety and Quality

- The research protocol should include a section that specifically addresses the preparation (compounding) of the radioactive drug and the specific tests to be performed.

- FDA recommends the following:

  a) for non-PET drugs, a stepwise, incremental approach to cGMP,

  b) for PET drugs, follow USP <823> until cGMPs for PET drugs are published.

FDA's RDRC Website

Information about FDA's Radioactive Drug Research Committee RDRC program can be found at the following web address:

http://www.fda.gov/cder/regulatory/RDRC/default.htm